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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/916,486	07/27/2001	Itzhak Ofek	2290.00123	1947

7590 05/10/2004

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EXAMINER	
CELSA, BENNETT M	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,486	OFEK ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 16-21* is/are pending in the application.

4a) Of the above claim(s) *2* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 16-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-2 and 16-21 are currently pending.

Claims 1 and 16-21 are currently under consideration.

Claims 2 is withdrawn from consideration as being directed to a nonelected invention.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1 and 16-21) in Paper No. 6 is again acknowledged. The requirement was made FINAL.

2. Claims 2 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

This application contains claim 2 drawn to a nonelected invention. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

Applicant's arguments that the present application fully complied with obtaining the benefit of an earlier filing date under 35 U.S.C. 120 of the 09/159,626 (9/2/4/98) application was persuasive. It is noted however, that the priority to the 08/772,021 is still denied.

Withdrawn Objection (s) and/or Rejection (s)

Aplicant's amendment has overcome the objection to claim 16 presented in the prior office action.

The submission of a terminal disclaimer of 6,303,125 and 5,840,322 has ovecome the following double patenting rejections:

a. Claims 1 and 16-18 over claims 1-10 of U.S. Patent No. 5,840,322 in view of '322 examples (e.g. to PF-1, PF-2 and NDM) and applicant's own specification (e.g. examples/figures) as evidence of inherency; and

b. Claims 1 and 16-21 over claims 1-3 of U.S. Patent No. 6,303,125 (10/16/01) and its disclosure (e.g. examples) as evidence of inherency.

In light of applicant's arguments and upon further consideration, the rejection of claims 1 and 16-21 under 35 U.S.C. 103(a) as being unpatentable over Ofek et al., "Anti-Escherichia Coli Adhesion Activity of Cranberry and Blueberry Juices", Toward Anti-Adhesion Therapy for Microbial Diseases, edited by Kahane and Ofek (Plenum Press, N.Y. 1996) pages 179-183, the specification **AND** Walker et al. US Pat. No. 5,525,341 (6/96: filed 2/94 or earlier) is hereby withdrawn (emphasis provided).

Outstanding Objection (s) and/or Rejection (s)

3. Claims 1 and 17-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1 and 19 (and claims dependent thereon), the molecular weight (MW) limitation is indefinite regarding the units (e.g. daltons, kilodaltons etc.) And the means used to measure molecular weight (e.g. gel chromatograph? Or acidic or basic PAGE conditions?). The means and conditions of MW measurement are important since different weight amounts may result from different means of measurement.

Discussion

Applicant's amendment and argument directed to the above indefinite rejection was considered but deemed nonpersuasive for the following reasons.

Applicant's amendment inserting the molecular weight units (e.g. kDa) fails to overcome the above indefinite rejection since the means of obtaining such a measurement is not given.

Accordingly, the above indefinite rejection is hereby maintained.

4. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (LACK OF WRITTEN DESCRIPTION).

Claim 16 (as amended) is directed to a pharmaceutical composition comprising pharmaceutical acceptable carriers/diluents and :

a. an isolated vaccinium juice fraction of MW $\geq$ 14,000 kDa (dialysis determined);

b. having anti-adhesion activity against H. pylori; and

c. capable of being added to a food drink.

Accordingly, the claimed composition is devoid of:

a. any composition structure whatsoever;

b. or any specific isolation protocol

but defines the composition as being "an isolated adhesion inhibitory fraction from vaccinium of MW $\geq$ 14,000 kDa" which has "anti-adhesion activity against H. pylori. E.g. applicant's claimed isolated compostion is defined in a purely functional manner.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

In the present instance, the claimed invention contains no identifying characteristics regarding chemical structure; and the small number of species PF-1, PF-2 and NDM defined by their method of isolation and/or a defined set of physicochemical properties (e.g. MW ; elemental analysis NMR, UV etc.) is not representative of the presently claimed composition.

In this regard, applicant is referred to *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) (and subsequent cases) and the

resulting "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001). It is additionally noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co*

With regard to the description requirement, Applicants' attention is further directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)]. In Eli Lilly, the specification and generic claims to all cDNAs encoding for vertebrate or mammalian insulin did not describe the claimed genus because they did not set forth any common features possessed by members of the genus that distinguished them from others. Id. At 1568, 43USPQ2d at 1405. Nor did the specification describe a sufficient number of species within the very broad genus to

indicate that the inventors had made a generic invention, i.e., that they had possession of the breadth of the genus, as opposed to merely one or two such species. E.g. See *Enzo Biochem. Inc.v. Gen-Probe Inc.*, Case No. 01-1230 (Fed. Cir. July 15, 2002) ("EnzoII"). Accordingly, the claimed pharmaceutical composition lacks written description.

Discussion

Applicant's amendment and argument directed to the above written description rejection was considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the above rejection was modified in response to applicant's amendment.

Applicant argues that amending claim 16 to insert "specific composition structure" provides adequate written description.

This argument was considered but deemed nonpersuasive for the following reasons and for the reasons provided in the rejection above. The presently claimed pharmaceutical composition broadly comprises an isolated vaccinium juice fraction of MW $\geq$ 14,000 kDa (dialysis determined); having anti-adhesion activity against H. pylori; which is capable of being added to a food drink. Accordingly, the claimed composition is devoid of any composition structure whatsoever or any specific isolation protocol and applicant's claimed isolated compostion is defined in a purely functional manner. The Examples presented in the specification simply are not representative of such a broadly claimed generic of isolated compositions as presently claimed.

Accordingly, the above rejection is hereby maintained.

5. Claims 1 and 16–18 are rejected under 35 U.S.C. 102(b) as anticipated, or alternatively obvious over Ofek et al., "Anti-Escherichia Coli Adhesion Activity of Cranberry and Blueberry Juices", Toward Anti-Adhesion Therapy for Microbial Diseases, edited by Kahane and Ofek (Plenum Press, N.Y. 1996) pages 179-183 alone or if necessary further in view of the present specification (e.g. specificatoin pages 16 and 28, examples and figures) to provide evidence of inherency. See MPEP 2131.01(d).

Claim 16 (as amended) is directed to a pharmaceutical composition comprising pharmaceutical acceptable carriers/diluents and :

a. an isolated vaccinium juice fraction of MW $\geq$ 14,000 kDa (dialysis determined);

b. having anti-adhesion activity against H. pylori; and

c. capable of being added to a food or drink.

In claims 1 and 18, the isolated vaccinium juice fraction is further described as having:

MW >= 14,000; by possessing carbon (43-51%) and hydrogen (4-5%) with no nitrogen/sulfur/chlorine and NMR/UR spectra; coaggregation reversal/inhibition; adhesion inhibition against P fimbriated bacteria/oral bacteria and inhibitory fraction of between 1 microgram and 10 mg/ml. Claim 17 claims the fraction which includes **PF-1**, PF-2 and NDM (emphasis provided). Claim 1 was similarly amended as claim 16 to be "capable of being added to a food or drink".

The Ofek et al. reference discloses a water-eluted fraction (e.g. PF-1; 100 mg: see e.g. Table 1) isolated from cranberry/blueberry juices (e.g. vaccinium juice) which appears to be identical to the composition presently claimed and which possesses

pharmaceutical activity (e.g. anti-adhesion). Accordingly, the reference meets the critical pharmaceutical composition claim limitations; and other parameters not specifically recited by the reference (e..g NMR/UV: *anti-H.pylori* etc.) would be deemed to be *inherently present* in a composition which is identical to that presently claimed. Additionally, the present specification (e.g. examples/figures) demonstrate that the PF-1 prior art fraction inherently possesses the same molecular weight; physicochemical parameters (e.g. NMR/IR etc.) and pharmaceutic inhibitory and (anti) aggregation activities as presently claimed.

With regard to the newly amended claims (e.g. claims 1and 16 , as amended) reciting that the isolated vaccinium juice fraction of MW $\geq$ 14,000 kDa (dialysis determined) be "capable of being added to a food drink" it is first noted that intended use language is NOT afforded patentable weight in compound/compositions claims as in the present case. Accordingly, this limitation need not be taught by the reference.

Alternatively applicant's own specification teaches that the reference composition is "capable of being added to a food drink" thus rendering this feature *inherent* to the reference compositions. Particularly, the present specification (e.g. at page 16 and especially page 28) teaches that the isolated reference fraction PF1 is capable of being added to a food or drink. For example, the specification at page 16 recites: .

> In the method of treating S. pylori infection in patients with such infections or with other bacterial infections that would benefit from the composition, the anti-adhesion fraction, PF-1, PF-2 or NMD, can be administered in various ways suitable for gastro- intestinal therapy. It should be noted that it can be administered as the compound or as pharmaceutically acceptable salt and can be administered alone or as an active ingredient in combination with pharmaceutically acceptable carriers, diluents, adjuvants and vehicles. The composition will **generally be administered orally**. Conventional methods such

> as administering the compounds in tablets, **suspensions, solutions, emulsions, capsules, powders, syrups** and the like are usable. Known techniques which deliver the anti-adhesion composition orally or intravenously and retain the biological activity are preferred.
>
> Additionally, and more specifically page 28 recites the following:
>
> The present invention also provides for a fortified food composition for oral hygiene comprising a suitable food carrier and an effective amount of an isolated adhesion inhibitory fraction from Vaccinium. In a preferred embodiment the food carrier is a fruit juice and the isolated adhesion inhibitory fraction is PF-1. The food carrier is selected sudh that does not decrease the biological activity of the present invention. The concentration of the adhesion inhibitory fraction the food carrier is between 10 pg/ml and 10 mg/ml or the equivalent weight/volume concentration for non-liquid foods. See specification page 28.

Accordingly, the specification on page 16 teaches that PF-1 can be administered in oral dosage forms (E.g. suspensions, solutions, emulsions, powders, syrups etc.) which are "capable of being added to a food or drink" and more spefically specification page 28 recited above explicitly teaches the use of PF-1 as a food/drink supplement.

The prior art appears to teach PF-1 amounts within the broad range (e.g. 1 microgram to 10 mg/ml) of the presently claimed invention. Alternatively, with regard to claim 1, to the extent that the amounts of the active agent are not specifically taught (e.g. 1 microgram to 10 mg/ml) it is noted that Ofek et al. specifically recognizes that "cranberry juices" (and their contained components) are recommended by physicians e.g. to prevent/treat urinary infections (e.g. see Ofek at pages 179-180); accordingly, the making of pharmaceutical compositions and the determination of optimum dosages is well within the skill of the art and thus would be obvious to one of ordinary skill at the time of applicant's invention.

Discussion

Applicant's amendment and arguments directed to the above 102/103 rejection were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the above rejection was modified in response to applicant's amendment.

Applicant argues that in view of the Ofek et al. reference and what is disclosed in the specification, it would not be obvious to make food or drink compositions comprising the Ofek et al. PF-1 composition. Particularly, applicant argues that E coli adhesion (taught by Ofek et al.) is different from that of oral bacteria as confirmed by PF-1 specification data evidence (e.g. regarding inhibit/reverse coaggregation of selected bacterial pairs). Additionally, applicant argues that "There is no indication that merely introducing this (PF-1) composition to a juice composition would be as simple as indicated in the Office action" since the present specification teaches that PF-1 is insoluble in butanol/ethylacetate and is acid precipitable and "loses partial activity upon heating in acidic solutions".

Applicant's arguments were considered but deemed nonpersuasive for the reasons recited in the above anticipation rejection. In this regard it is noted that applicant's arguments directed against obviousness fail to address anticipation.

As pointed out in the rejection above, the newly amended claims (e.g. claims 1and 16 , as amended) recite that the isolated vaccinium juice fraction of MW $\geq$ 14,000 kDa (dialysis determined) be "capable of being added to a food drink".

In this respect it is first noted that intended use language is NOT afforded patentable weight in compound/compositions claims as in the present case. Accordingly, this limitation need not be taught by the reference.

Alternatively applicant's own specification teaches that the reference composition is **inherently** "capable of being added to a food drink". Particularly, the present specification (e.g. at page 16 and especially page 28) teaches that the isolated reference fraction PF1 is capable of being added to a food or drink. For example, the specification at page 16 recites: .

> In the method of treating S. pylori infection in patients with such infections or with other bacterial infections that would benefit from the composition, the anti-adhesion fraction, PF-1, PF-2 or NMD, can be administered in various ways suitable for gastro- intestinal therapy. It should be noted that it can be administered as the compound or as pharmaceutically acceptable salt and can be administered alone or as an active ingredient in combination with pharmaceutically acceptable carriers, diluents, adjuvants and vehicles. The composition will **generally be administered orally**. Conventional methods such as administering the compounds in tablets, **suspensions, solutions, emulsions, capsules, powders, syrups** and the like are usable. Known techniques which deliver the anti-adhesion composition orally or intravenously and retain the biological activity are preferred.

Additionally, and more specifically page 28 recites the following:

> The present invention also provides for a fortified food composition for oral hygiene comprising a suitable food carrier and an effective amount of an isolated adhesion inhibitory fraction from Vaccinium. In a preferred embodiment the food carrier is a fruit juice and the isolated adhesion inhibitory fraction is PF-1. The food carrier is selected sudh that does not decrease the biological activity of the present invention. The concentration of the adhesion inhibitory fraction the food carrier is between 10 pg/ml and 10 mg/ml or the equivalent weight/volume concentration for non-liquid foods. See specification page 28.

Accordingly, the specification on page 16 teaches that PF-1 can be administered in oral dosage forms (E.g. suspensions, solutions, emulsions, powders, syrups etc.) which are "capable of being added to a food or drink"; and more particularly specification page 28 teaches the use of PF-1 as a food/drink supplement.

Additionally, to the extent that applicant argues that the Ofek et al. reference fails to appreciate Applicant's discovered utility (e.g. food/drink fortification) this argument is not persuasive since the present claims recite that the composition only need be "capable of being added to a food or drink" which would be inherent to a composition which otherwise meets applicant's claimed components and amounts as discussed in the rejection.

Further, with regard to the obviousness of claim 1, the Ofek et al. prior art reference needs only to render obvious (e.g. with regard to adhesion inhibitory fraction amounts) the claimed composition (albeit for a different reason e.g. to prevent/treat urinary infections), since it is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. In re Linter , 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) ; In re Dillon , 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied , 500 U.S. 904 (1991); MPEP 2144.

Thus, the above modified rejection is hereby maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Future Correspondences

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 703-305-7556. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 703-306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
May 3, 2003